Figure 26: Schematic diagram illustrating systems for forming assemblies of CdSe/ZnS core/shell quantum dots (QD).

Figures 27A-D: Figure 27A shows fluorescence spectra comparing dispersed and aggregated QDs, with an excitation at 400 nm. The samples were prepared identically, except for the addition of complementary "linker" DNA to one and an equal volume and concentration of non-complementary DNA to the other. Figure 27B shows UV-Visible spectra of QD/QD assemblies at different temperatures before, during and after "melting". Figure 27C shows high resolution TEM image of a portion of a hybrid gold/QD assembly. The lattice fringes of the QDs, which resemble fingerprints, appear near each gold nanoparticle. Figure 27D shows UV-Visible spectra of hybrid gold/QD assemblies at different temperatures before, during and after "melting". The insets in Figures 27B and 27D display temperature versus extinction profiles for the thermal denaturation of the assemblies. Denturation experiments were conducted in 0.3 M NaCl, 10 mM phosphate buffer (pH 7), 0.01% sodium azide with 13 nm gold nanoparticles and/or ~4 nm CdSe/ZnS core/shell QDs.

Figures 28A-E: Schematic diagrams illustrating the preparation of core probes, aggregate probes and systems for detecting DNA using these probes. In these figures, a, b, c and d refer to different oligonucleotide sequences, and a', b', c' and d' refer to oligonucleotide sequences complementary to a, b, c and d, respectively.

Figure 29: Graph of fractional displacement of oligonucleotides by mercaptoethanol from nanoparticles (closed circles) or gold thin films (open squares) to which the oligonucleotides had been attached.

Figure 30: Graph of surface coverages of recognition oligonucleotides on nanoparticles obtained for different ratios of recognition:diluent oligonucleotides used in the preparation of the nanoparticle-oligonucleotide conjugates.

Figure 31: Graph of surface coverages of hybridized complementary oligonucleotides versus different surface coverages of recognition oligonucleotides on nanoparticles.

Figure 32: Schematic diagram illustrating system for detecting a target DNA in a four-element array on a substrate using nanoparticle-oligonucleotide conjugates and amplification with silver staining.

Figure 33: Images obtained with a flatbed scanner of 7 mm x 13 mm oligonucleotide-functionalized float glass slides. (A) Slide before hybridization of DNA target and gold nanoparticle-oligonucleotide indicator conjugate. (B) Slide A after hybridization of 10 nM target DNA and 5 nM nanoparticle-oligonucleotide indicator conjugate. A pink color was imparted by attached, red 13 nm diameter gold nanoparticles. (C) Slide B after exposure to silver amplification solution for 5 minutes. (D) Same as (A). (E) Slide D after hybridization of 100 pM target and 5 nM nanoparticle-oligonucleotide indicator conjugate. The absorbance of the nanoparticle layer was too low to be observed with the naked eye or flatbed scanner. (F) Slide E after exposure to silver amplification solution for 5 minutes. Note that slide F is much lighter than slide C, indicating lower target concentration. (G) Control slide, exposed to 5 nM nanoparticle-oligonucleotide indicator conjugate and exposed to silver amplification solution for 5 minutes. No darkening of the slide was observed.

Figure 33: Graph of greyscale (optical density) of oligonucleotide-functionalized glass surface exposed to varying concentrations of target DNA, followed by 5 nM gold of nanoparticle-oligonucleotide indicator conjugates and silver amplification for 5 minutes.

Figures 35A-B: Graphs of percent hybridized label versus temperature showing dissociation of fluorophore-labeled (Figure 35A) and nanoparticle-labeled (Figure 35B) targets from an oligonucleotide-functionalized glass surface. Measurements were made by measuring fluorescence (Figure 35A) or absorbance (Figure 35B) of dissociated label in the solution above the glass surface. The lines labeled "b" show the dissociation curves for perfectly matched oligonucleotides on the glass, and the lines labeled "r"show curves for mismatched oligonucleotides (a one-base mismatch) on the glass. Vertical lines in the graphs illustrate the fraction of target dissociated at a given temperature (halfway between the melting temperatures T_m of each curve) for each measurement, and the expected selectivity of sequence identification for fluorophore- and nanoparticle-based gene chips.

Fluorescence (Figure 35A): complement (69%)/mismatch (38%) = 1.8:1. Absorbance (Figure 35B): complement (85%)/mismatch (14%) = 6:1. The breadth of the fluorophore-labeled curves (Figure 35A) is characteristic of the dissociation of fluorophore-labeled targets from gene chips (Forman et al., in *Molecular Modeling of Nucleic Acids*, Leontis et al., eds., (ACS Symposium Series 682, American Chemical Society, Washington D.C., 1998), pages 206-228).

Figures 36A-B: Images of model oligonucleotide arrays challenged with synthetic target and fluorescent-labeled (Figure 36A) or nanoparticle-labeled (Figure 36B) nanoparticle-oligonucleotide conjugate probes. C, A, T, and G represent spots (elements) on the array where a single base change has been made in the oligonucleotide attached to the substrate to give a perfect match with the target (base A) or a single base mismatch (base C, T or G in place of the perfect match with base A). The greyscale ratio for elements C:A:T:G is 9:37:9:11 for Figure 36A and 3:62:7:34 for Figure 36B.

Figure 37: Schematic diagram illustrating system for forming aggregates (A) or layers (B) of nanoparticles (**a** and **b**) linked by a linking nucleic acid (**3**).

Figure 38A: UV-visible spectra of alternating layers of gold nanoparticles ***a*** and ***b*** (see Figure 37) hybridized to an oligonucleotide-functionalized glass microscope slide via the complementary linker **3**. The spectra are for assemblies with 1 (**a**, λ_{max} = 524 nm), 2 (**b**, λ_{max} = 529 nm), 3 (**c**, λ_{max} = 532 nm), 4 (**d**, λ_{max} = 534 nm) or 5 (**e**, λ_{max} = 534 nm) layers. These spectra were measured directly through the slide.

Figure 38B: Graph of absorbance for nanoparticle assemblies (see Figure 38A) at λ_{max} with increasing numbers of layers.

Figures 39A-F: Figure 39A: FE-SEM of one layer of oligonucleotide-functionalized gold nanoparticles cohybridized with DNA linker to an oligonucleotide-functionalized, conductive indium-tin-oxide (ITO) slide (prepared in the same way as oligonucleotide-funcationalized glass slide). The visible absorbance spectrum of this slide was identical to Figure 38A, indicating that functionalization and nanoparticle coverage on ITO is similar to that on glass. The average density of counted nanoparticles from 10 such images was